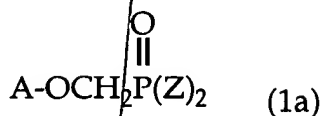


CLAIMS

We claim:

1. A compound having formula (1a)



wherein Z is independently $-\text{OC}(\text{R}^2)_2\text{OC}(\text{O})\text{X}(\text{R})_a$, an ester, an amidate or $-\text{H}$, but at least one Z is $-\text{OC}(\text{R}^2)_2\text{OC}(\text{O})\text{X}(\text{R})_a$;

A is the residue of an antiviral phosphonomethoxy nucleotide analog;

X is N or O;

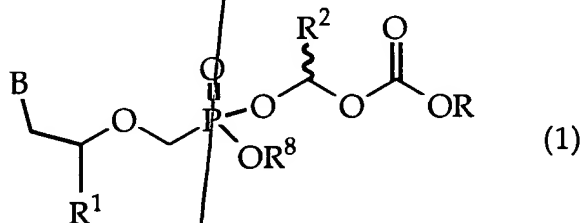
R^2 independently is $-\text{H}$, C_1 - C_{12} alkyl, C_5 - C_{12} aryl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, C_7 - C_{12} alkenylaryl, C_7 - C_{12} alkynylaryl, or C_6 - C_{12} alkaryl, any one of which is unsubstituted or is substituted with 1 or 2 halo, cyano, azido, nitro or $-\text{OR}^3$ in which R^3 is C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl or C_5 - C_{12} aryl;

R is independently $-\text{H}$, C_1 - C_{12} alkyl, C_5 - C_{12} aryl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, C_7 - C_{12} alkenylaryl, C_7 - C_{12} alkynylaryl, or C_6 - C_{12} alkaryl, any one of which is unsubstituted or is substituted with 1 or 2 halo, cyano, azido, nitro, $-\text{N}(\text{R}^4)_2$ or $-\text{OR}^3$, where R^4 independently is $-\text{H}$ or C_1 - C_8 alkyl, provided that at least one R is not H; and

a is 1 when X is O, or 1 or 2 when X is N;

with the proviso that when a is 2 and X is N, (a) two N-linked R groups can be taken together to form a carbocycle or oxygen-containing heterocycle, (b) one N-linked R additionally can be $-\text{OR}^3$ or (c) both N-linked R groups can be $-\text{H}$; and the salts, hydrates, tautomers and solvates thereof.

2. The compound of claim 1 having formula (1)



wherein B is guanine-9-yl, adenine-9-yl, 2,6-diaminopurine-9-yl, 2-aminopurine-9-yl or their 1-deaza, 3-deaza, or 8-aza analogs, or B is cytosine-1-yl;

R is independently -H, C₁-C₁₂ alkyl, C₅-C₁₂ aryl, C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, C₇-C₁₂ alkenylaryl, C₇-C₁₂ alkynylaryl, or C₆-C₁₂ alkaryl, any one of which is unsubstituted or is substituted with 1 or 2 halo, cyano, azido, nitro or -OR³ in which R³ is C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl or C₅-C₁₂ aryl;

R¹ is hydrogen, -CH₃, -CH₂OH, -CH₂F, -CH=CH₂, or -CH₂N₃, or R¹ and R⁸ are joined to form -CH₂-;

R² independently is hydrogen or C₁-C₆ alkyl; and

R⁸ is hydrogen or -CHR²-O-C(O)-OR, or R⁸ is joined with R¹ to form -CH₂-;

and the salts, hydrates, tautomers and solvates thereof.

3. The compound of claim 2 wherein R² is -H.

4. The compound of claim 3 wherein R¹ is -CH₃.

5. The compound of claim 1 wherein R² is -H.

6. The compound of claim 1 wherein one R² is -CH₃ and the other R² is H.

7. The compound of claim 1 wherein R³ is C₁-C₆ alkyl or phenyl.

8. The compound of claim 1 wherein R³ is -CH₃ or -C₂H₅.

9. The compound of claim 1 wherein X is O.

10. The compound of claim 1 wherein X is N and one R³ is H.

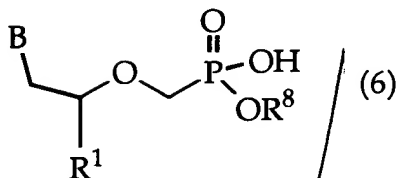
11. The compound of claim 4 wherein the compound is enriched or resolved at the carbon atom chiral center linked to R¹.

12. The compound of claim 4 wherein at least about 90% of the compound is in the (R) configuration at the R¹ site.

13. The compound of claim 12 wherein B is adenin-9-yl.

14. The compound of claim 13 wherein each R is ethyl.

15. The compound of claim 13 wherein each R is isopropyl.
16. The compound of claim 13 wherein each R is 3-pentyl or neopentyl.
17. The compound of claim 13 wherein each R is *t*-butyl or isobutyl.
18. The compound of claim 4 wherein B is 2,6-diaminopurin-9-yl.
19. The compound of claim 3 wherein R¹ is H.
20. The compound of claim 19 wherein B is adenin-9-yl.
21. The compound of claim 4 wherein R is C₁-C₁₂ alkyl.
22. The compound of claim 3 wherein R¹ is -CH₂OH.
23. The compound of claim 22 wherein B is cytosin-1-yl.
24. The compound of claim 1 named in Table B and compound groups 1-19.
25. The compound of claim 22 wherein at least about 90% of the compound is in the (*S*) configuration at the R¹ site.
26. A method comprising orally administering to a patient infected with virus or at risk to viral infection a therapeutically effective amount of a compound of claim 1.
27. A method for preparing a compound of formula (1a) comprising reacting the diacid of a phosphonmethoxy nucleotide analog with L-CH(R²)OC(O)X(R)_n wherein L is a leaving group.
28. A method for preparing a compound of formula (1) comprising reacting a compound of formula (6)



with $L-CHR^2-O-C(O)-OR$ and recovering a compound of formula (1), wherein B is guanin-9-yl, adenin-9-yl, 2,6-diaminopurin-9-yl, 2-aminopurin-9-yl or their 1-deaza, 3-deaza, or 8-aza analogs, or B is cytosin-1-yl;

5 R^1 is hydrogen, $-CH_3$, $-CH_2OH$, $-CH_2F$, $-CH=CH_2$, $-CH_2N_3$ or R^1 and R^8 are joined to form $-CH_2-$; and

R^8 is hydrogen, $-CHR^2-O-C(O)-OR$ or R^8 is joined with R^1 to form $-CH_2-$; and

10 R^2 is H, C_1-C_{12} alkyl, aryl, alkenyl, alkynyl, alkyenylaryl, alkynylaryl, alkaryl, arylalkynyl, arylalkenyl or arylalkyl which is unsubstituted or is substituted with halo, azido, nitro or OR^3 in which R^3 is C_1-C_{12} alkyl;

15 R is independently H, C_1-C_{12} alkyl, aryl, alkenyl, alkynyl, alkyenylaryl, alkynylaryl, alkaryl, arylalkynyl, arylalkenyl or arylalkyl which is unsubstituted or is substituted with halo, azido, nitro or OR^3 , provided that at least one R is not H; and

L is a leaving group.

20 29. The method of claim 30 comprising conducting the reaction using at least about 1.0 equivalent of $L-CHR^2-O-C(O)-OR$.

30 30. The method of claim 31 comprising conducting the reaction in the presence of an organic base in an organic solvent at a reaction temperature of about $4-100^\circ C$ for about 4-72 hours.

25 31. The method of claim 28 wherein the compound of formula (1) is recovered by forming a salt, precipitating the salt and recovering the precipitated salt.

30 32. The method of claim 31 wherein the salt is formed from sulfuric acid, phosphoric acid, lactic acid, or citric acid.